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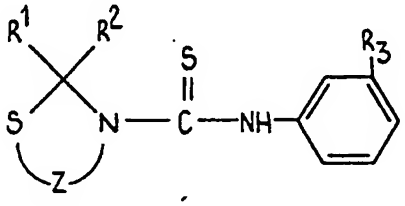
(54) **Novel heterocyclic carbothioamides, compositions containing them, their preparation and use**

(57) Novel 2-substituted-N-(3-substituted phenyl)thiazolidine-, tetrahydro-2H-1,3-thiazine-, and benzothiazoline-3-carbothioamides, which are useful as insecticides, have the formula I:-



wherein
R_1 is selected from various defined organic groups. R_2 is hydrogen or C_{1-3} alkyl, R_3 is halogen, $-CF_3$, -CN or $-OCF_2CF_2H$ and Z completes a thiazolidine, tetrahydro-2H-1, 3-thiazine or benzothiazoline ring. These compounds are prepared by reacting an appropriate phenyl isothiocyanate with an appropriately substituted thiazolidine, tetrahydro-2H-1,3-thiazine, or benzothiazoline.

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SPECIFICATION

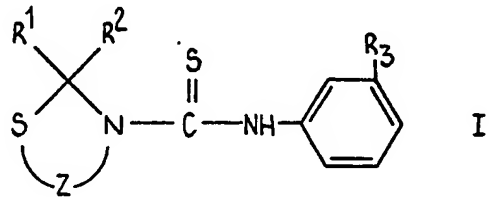
Novel heterocyclic carbothioamides, compositions containing them, their preparation and use

This invention relates to heterocyclic carbothioamides. More particularly, this invention relates to 2-substituted-N-(3-substituted phenyl)thiazolidine-, tetrahydro-2H-1,3-thiazine-, and benzothiazoline-3-carbothioamides which are useful as insecticides.

Compounds containing the thiazolidine nucleus are now new; see, *e.g.*, G.W. Stacy *et al., J. Org. Chem., 23,* 1760 (1958). Most of the 2-substituted thiazolidines appear to be 2-iminothiazolidines. The non-imino compounds, on the other hand, are primarily 2-thioureido-2-thiazolines. See, for example, E. Cherbuliez *et al., Helv.Chim. Acta, 49,* 807 (1966) [*Chem. Abstr., 64,* 158664D (1966)]; Y. Yamamoto *et al., Kyoritsu Yakka Daigaku Kerkyu Nempo, 1973,* 53 [*Chem. Abstr., 81*, 136039z (1974]; D.L. Klayman *et al., Tetrahedron Lett., 1967,* 281 [*Chem. Abstr., 66.,* 94943x (1967)]; D.L. Klayman *et al., J. Heterocycl. Chem., 5,* 517 (1968); S.P. Kharida *et al., J. Indian Chem. Soc., 37,* 305 (1960 [*Chem. Abstr., 55,* 10373a (1961)]; and D.L. Klayman *et al., Tetrahedron, 25,* 191 (1969). No utilities appear to have been disclosed for any of such compounds.

T.P. Forrest *et al., Can. J. Chem., 52,* 2725 (1974), disclose 5-methoxy-2-phenylamino-2-2-thiazoline. Again, no utilities are disclosed. Finally, R.E. Hackler *et al., Synthetic Communications, 5,* 143 (1975), disclose the formation of 2-substituted-2-thiazolines from haloalkyl isothiocyanates. Examples of such 2-substituents include dimethylamino, piperidino, and 4-methylpiperidino. No utilities were given.

In accordance with the present invention, heterocyclic carbothioamides are provided, having the formula,



I

wherein

R^1 is

(A) C_1–C_{18} alkyl;

(B) C_2–C_{18} alkenyl;

(C) C_4–C_{18} alkadienyl;

(D(C_3–C_{12} cycloalkyl, optionally substituted with either one or two C_1—C_3 alkyl groups;

(E) C_5–C_{12} cycloalkenyl, optionally substituted with either one or two C_1–C_3 alkyl groups;

(F) C_6–C_{12} cycloalkadienyl, optionally substituted with either one or two C_1–C_3 alkyl groups;

(G) phenyl, optionally substituted with from one to three groups selected from the group consisting of

(1) C_1–C_8 alkyl,

(2) C_1–C_8 alkoxy,

(3) C_1–C_8 alkylthio,

(4) trifluoromethyl,

(5) halo, and

(6) cyano;

(H) (cycloalkyl)alkyl, containing no more than about 18 carbon atoms, in which the cycloalkyl moiety is as defined hereinabove;

(I) phenylalkyl, containing no more than about 18 carbon atoms, in which the phenyl moiety is as defined hereinabove;

(J) diphenylalkyl, containing no more than about 18 carbon atoms, in which each phenyl moiety is as defined hereinabove;

(K) pyridyl, optionally substituted with either one or two groups selected from the group consisting of

(1) C_1–C_3 alkyl,

(2) C_1–C_3 alkoxy, or

(3) halo;

(L) piperidino attached at a position other than the nitrogen atom, optionally substituted with either one or two C_1–C_3 alkyl groups;

(M) morpholino attached at a position other than the nitrogen atom;

(N) pyrazinyl, optionally substituted with either one or two C_1–C_3 alkyl groups;

(O) pyridylalkyl, containing no more than about 17 carbon atoms, in which the pyridyl moiety is as defined hereinabove;

(P) piperidinoalkyl, contaning no more than about 17 carbon atoms, in which the piperidino moiety is as defined hereinabove;

(Q) morpholinoalkyl, containing no more than about 16 carbon atoms;

(R) pyrazinylalkyl, containing no more than about 16 carbon atoms, in which the pyrazinyl moiety is as

defined hereinabove; or

(S) tetrahydrofuryalkyl, containing no more than about 17 carbon atoms;

R^2 is hydrogen or C_1—C_3 alkyl;

R^3 is

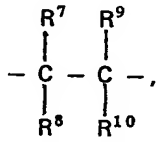
(A) halo,

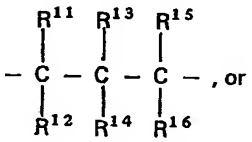
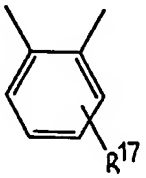
(B) trifluoromethyl,

(C) cyano, or

(D) 1, 1, 2, 2-tetrafluoroethoxy;

Z is

(A)  ,

(B)  , or (C) 

in which each of R^7—R^{16}, inclusive, independently is hydrogen or C_1—C_3 alkyl, with the proviso that the two groups attached to any given carbon atom in (A) or (B) together can not contain more than four carbon atoms; and

R^{17} is

(1) C_1–C_3 alkyl,

(2) C_1–C_3 alkoxy,

(3) C_1–C_3 alkylthio,

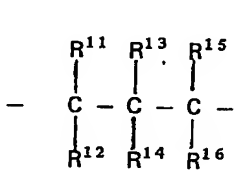
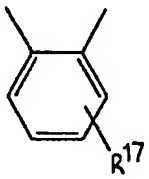
(4) trifluoromethyl,

(5) halo,

(6) cyano, or

(7) hydrogen;

with the proviso that when Z is

 or 

R^2 is hydrogen.

A preferred group of compounds comprises the compounds of formula I wherein

R^1 is

(1) alkyl,

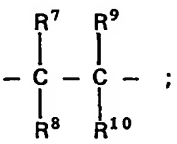
(2) phenyl, optionally monosubstituted with halo or C_1–C_3 alkyl, or

(3) phenylalkyl, in which the phenyl moiety is unsubstituted;

R^3 is halo or trifluoromethyl; and each of R^7–R^{17}, inclusive, is hydrogen.

Included within the above preferred group of compounds are the following more preferred embodiments:

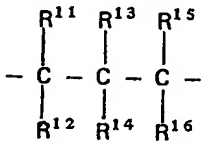
(1) Z is

 ;

R^1 is alkyl, benzyl, or phenyl which is optionally monosubstituted with bromo; and

R^3 is chloro or bromo;

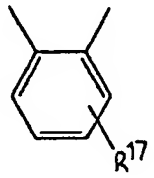
(2) Z is



;

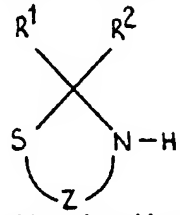
R^1 is alkyl or phenyl which is optionally monosubstituted with methyl, bromo, or chloro;
R^2 is hydrogen; and
R^3 is bromo, chloro, or trifluoromethyl;

(3)) Z is

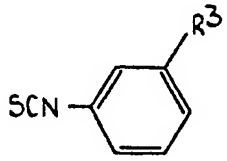


R^1 is C_1–C_3 alkyl;
R^2 is hydrogen; and
R^3 is bromo or chloro.

The compounds of formula I are prepared by reacting a compound of the formula



wherein R^1, R^2, and Z are defined as before, with a phenyl isothiocyanate of the formula



wherein R^3 is defined as before. This process is one of analogy is described in greater detail hereinafter.

The present invention also provides a method for reducing or eradicating a population of the insect species *Epilachna varivestis* which comprises administering to the insect by ingestion of insecticidally-effective amount of a compound of formula I.

Additionally, the present invention provides an insecticidal composition which comprises an insecticidally-effective amount of a compound of formula I and an agriculturally-acceptable carrier.

In formula I, the various chemical groups have their usual meanings. For the sake of clarity, however, examples of the various generally-named groups will be given.

The term "C_1–C_{18} alkyl" includes, among others, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, neopentyl, 1-methylbutyl, hexyl, isohexyl, 2, 3-dimethylbutyl, 1-ethylpentyl, 2-ethyl-3-methylbutyl, 2-ethylhexyl, 5-methylheptyl, nonyl, 2, 4,4-trimethylhexyl, decyl, 7,7-dimethyloctyl, 1-propylheptyl, 1,1-dimethyloctyl, undecyl, 3-ethyl-2,6-dimethylheptyl, 10-methylundecyl, 5-ethyl-2,6-dimethyloctyl, tridecyl, 2,2,6,6,7-pentamethyl-octyl, 9-ethyldodecyl, pentadecyl, 5-*sec*-butyl-2,7-dimethylnonyl,14-methylpentadecyl, 3-propyl-8-ethyldodecyl, octadecyl, and 1-methylheptadecyl.

The terms "C_2–C_{18} alkenyl" and "C_4–C_{18} alkadienyl" include, among others, vinyl, 1-propenyl, allyl, isopropenyl, 1-butenyl, 2-butenyl, 1-pentenyl, 2-pentenyl, 2-methyl-2-butenyl, 1-hexenyl, 2-hexenyl, 3-hexenyl, 4-methyl-1-pentenyl, 2-methyl-1-pentenyl, 2-methyl-2-pentenyl, 3-methyl-2-pentenyl, 2,3-dimethyl-2-butenyl, 3,3-dimethyl-1-butenyl, 1-heptenyl, 2-heptenyl, 4-methyl-1-hexenyl, 2, 4-dimethyl-1-pentenyl, 2-propyl-1-butenyl, 2,3,3-trimethyl-1-butenyl, 1-octenyl, 2-octenyl, 4-octenyl, 2, 4,4-trimethyl-1-pentenyl, 1-nonenyl, 2,3-diethyl-2-pentenyl, 1-decenyl, 5-decenyl, 3-isopropyl-3-heptenyl, 4-undecenyl, 1-dodecenyl, 2-methyl-1-undecenyl, 2,2,4,6,6-pentamethyl-3-heptenyl, 1-tridecenyl, 3-tetradecenyl, 5-pentadecenyl, 1-hexadecenyl, 1,5-dimethyl-2-ethyl-3-propyl-4-nonenyl, 1-octadecenyl, 1,3-butadienyl, 1,3-pentadienyl, 1,4-pentadienyl, 2-methyl-1,3-butadienyl, 3-methyl-1,2-butadienyl, 1,2-hexadienyl, 1,4-hexadienyl, 1,5-hexadienyl, 2,4-hexadienyl, 2-ethyl-1,3-butadienyl, 2-methyl-1,3-pentadienyl, 4-methyl-

1,3-pentadienyl,2,3-dimethyl-1,3-butadienyl, 1,4-heptadienyl, 1,6-heptadienyl, 2,4-dimethyl-1,3-pentadienyl, 1,7-octadienyl, 2,5-dimethyl-2,4-hexadienyl, 1,8-nonadienyl, 7-methyl-2,4-octadienyl, 1,3-decadienyl, 2,6-dimethyl-2,6-octadienyl, 1,10-undecadienyl, 5,6-dimethyl-4-ethyl-1,2-heptadienyl, 1,5-dodecadienyl, 1,12-tridecadienyl, 4-isopropyl-1,9-decadienyl, 6,8-tetradecadienyl, 6,9-pentadecadienyl, 1,15-hexa-decadienyl, 6,10-hexadecadienyl, 2,3,11-trimethyl-6,9-tridecadienyl, 7,10-heptadecadienyl, 1,17-octadecadienyl, and 2-methyl-7,10-heptadecadienyl.

The term "C_1-C_3 alkyl" includes methyl, ethyl, propyl, and isopropyl. Thus, the phrase "C_3-C_{12} cycloalkyl, optionally substituted with either one or two C_1-C_3 alkyl groups" is meant to include, among others, such groups as cyclopropyl, 2-ethylcylopropyl, cyclobutyl, 2,3-dimethylcyclo-butyl, cyclopentyl, cyclobutyl, 2,3-dimethylcyclo-butyl, cyclopentyl, 3-propylcyclopentyl, cyclohexyl, 2-methyl-4-isopropylcyclohexyl, cycloheptyl, 3-ethylcycloheptyl, cyclooctyl, cyclononyl, 3,5-diisopropylcyclononyl, cyclodecyl, 1-methyl-4-ethylcyclodecyl, cycloundecyl, and cyclododecyl.

The phrases "C_5-C_{12} cycloalkenyl, optionally substituted . . ." and "C_6-C_{12} cycloalkadienyl, optionally substituted..." are meant to include, among others, such groups as cyclopentenyl, 2-ethylcyclopentenyl, cyclohexenyl, 4-methycyclo-hexenyl, 2-isopropyl-5-methylcyclohexenyl, cycloheptenyl, cyclooctenyl, 3,5-dimethylcyclooctenyl, cyclononenyl, 2-ethylcyclononenyl, cyclodecenyl, 4-isopropyl-7-methylcyclodecenyl, cycloundecenyl, 5-methylcycloundecenyl, cyclododecenyl, 3-propylcyclo-dodecenyl, 1,3-cyclohexadienyl, 5-methyl-1,3-cyclohexadienyl, 1,4-cyclohexadienyl, 1,3-cyclo-heptadienyl, 2,4-dimethyl-1,3-cycloheptadienyl, 2,4-cycloheptadienyl, 1,3-cyclooctadienyl, 1,4-cyclooctadienyl, 1,5-cyclooctadienyl, 1-methyl-2,5-cyclooctadienyl, 1,4-cyclononadienyl, 3,6-dipropyl-1,3-cyclononadienyl, 1,3-cyclodecadienyl, 3-ethyl-1,5-cyclodecadienyl, 2,5-cycloundecadienyl,4-ethyl-5-methyl-1,7-cycloundecadienyl, 1,3-cyclo-dodecadienyl, 1,7-cyclodecadienyl, and 3-propyl-2,5-cyclododecadienyl.

The term "C_1–C_6 alkyl" and the alkyl moiety in the terms "C_1-C_6 alkylthio" and "C_1-C_6 alkoxy" include, for example, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *t*-butyl, pentyl, isopentyl, 1-methylbutyl, 1-ethylpropyl, neopentyl, hexyl, isohexyl. Similarly, the phrase "phenyl, optionally substituted with . . ." is meant to include, among others, such groups as phenyl, *m*-tolyl, *o*-cumenyl, 4-hexylphenyl, 3-trifluoromethylphenyl, 3-isobutylthio-phenyl, 2-ethoxyphenyl, 2-fluorophenyl, 3-chlorophenyl, 4-bromophenyl, 3-iodophenyl, 4-cyanophenyl, 2,6-xylyl, 2,4-bis(trifluoromethyl)phenyl, 2-methyl-thio-4-butylthiophenyl, 2,3-dimethoxyphenyl, 3,5-dichlorophenyl, 2-bromo-5-chlorophenyl, 3,4-dicyano-phenyl, 3-trifluoromethyl-5-neopentylphenyl, 5-fluoro-2-methoxyphenyl, mesityl, 4-bromo-3,5-dimethyl-phenyl, 2-methyl-4-cyano-5-pentylphenyl, 2,5-dichloro-4-fluorophenyl, and 2,4,6-triethoxyphenyl.

The phrase "(cycloalkyl)alkyl, containing . . ." includes, among others, cyclopropylmethyl, 6-(2-ethylcyclopropyl)hexyl, 2,3-dimethylcyclobutylmethyl, 7-cyclopentyl-2,2-dimethyloctyl, cyclohexylmethyl, 3-(3)isopropylcyclohexyl)propyl, 2-(1-methyl-4-ethylcyclooctyl)ethyl, and 4-cycloundecylpentyl.

The phrases "phenylalkyl, containing . . ." and "diphenyalkyl, containing . . ." include, among others, benzyl, phenethyl, 4-(*o*-cumenyl)octyl, 3-(2)methyl-4-isohexyloxphenyl)butyl, 1,3-dimethyl-6-(2-cyano-3-ethyl-5-fluorophenyl-heptyl, diphenyl-methyl, and 2-methyl-2-(*m*-tolyl)-3-(2,4-dichlorophenyl)propyl.

The phrase "pyridyl, optionally substituted . . ." includes, among others, 2-pyridyl, 3-pyridyl, 2-methyl-4-pyridyl, 5-ethoxy-3-pyridyl, 2,6-dichloro-4-pyridyl, and 2-ethyl-5-methyl-3-pyridyl.

The phrases "piperidino . . . optionally substituted . . ." and "pyrazinyl, optionally substituted . . ." include, among others, 3-piperidino, 2,5-dimethyl-4-piperidino, 4-isopropyl-2-piperidino, 2-pyrazinyl, 5-ethyl-2-pyrazinyl, and 3,5-dimethyl-2-pyrazinyl.

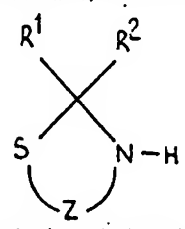
The phrases "pyridylalkyl, containing . . .", "piperidinoalkyl, containing . . .", "morpholinoalkyl, containging . . .", "pyrazinylalkyl, containing . . ." and "tetrahydrofurylalkyl, containing . . ." include, among others, 2-pyridylmethyl, 4-(4-pyridyl)heptyl, 2,2-dimethyl-3-(3,5-dimethoxy-2-pyridyl)propyl, 11-(2-piperidino)undecyl, 4-ethyl-4-(2-ethyl-4-piperidino)-butyl, 1,1-dimethyl-2-(morpholino)ethyl, 1-ethyl-3-(3,6-dimethyl-2-pyrazinyl)propyl, (5-propyl-2-pyrazinyl)methyl, 4-tetrahydrofurylbutyl, and 2-ethyl-5-tetrahydrofurylpentyl.

In order to clarify the present invention, the following list of compounds is given by way of illustration. It is to be understood, however, that the present invention is neither confined to nor limited by the compounds listed.

1. 2-(2-ethylhexyl)-N-(3-fluorophenyl)-3-thiazolidinecarbothiomide,
2. N-(3-bromophenyl)-2-(3-isopropyl-1-methylundecyl)-2,4,5-triethyl-3-thiazolidinecarbothioamide,
3. 2-octadecyl-N-[3-)1,1,2,2-tetrafluoroethoxy)phenyl]-3-thiazolidinecarbothioamide,
4. N-(3-chlorophenyl)-2-cyclopentyl-4-ethyl-4-methyl-3-thiazolidinecarbothioamide,
5. N-(3-cyanophenyl)2-(4-methylcyclononyl)-3-thiazolidinecarbothioamide,
6. N-(3-iodphenyl–2-(4-iodophenyl)-3-thiazolidinecarbothioamide,
7. N-(3-chlorophenyl)-2-(5-cyclopropyl-3-ethylhexyl-3-thiazolidinecarbothioamide,
8. 2-isopropyl-2-(2-methyl-2-phenylpropyl)-5-ethyl-N-(3-trifluoromethylphenyl)-3-thiazolidine-carbothioamide,
9. 2-[2-(2,4-dimethoxy-5-cyanophenyl)-ethyl]-4,5-dimethyl-N-(3-fluorophenyl)-3-thiazolidine-carbothioamide,
10. 2-(2,4-diphenylbutyl)-N-(3-iodophenyl)-4-propyl-3-thiazolidinecarbothioamide,

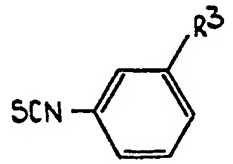
11. N-(3-bromophenyl)-2-(2-chloro-5-ethoxy-4-pyridyl)-3-thiazolidinecarbothioamide,
12. N-(3-bromophenyl)-5-methyl-2-piperidino-methyl-3-thiazolidinecarbothioamide,
13. N-(3-chlorophenyl)-5-ethyl-2-(3-ethyl-7,7-dimethyl-5-morpholinooctyl)-3-thiazolidinecarbothioamide,
14. N-(3-cyanophenyl)-2-[2-ethyl-4-(3-tetrahydrofuryl)hexyl]-3-thiazolidinecarbothioamide,
15. N-(3-bromophenyl)-2-methyl-4-isopropyl-3-thiazolidinecarbothioamide,
16. 2-hexyl-N-[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-3-thiazolidinecarbothioamide,
17. 2-benzyl-2-ethyl-N-(3-fluorophenyl)-3-thiazolidinecarbothioamide,
18. N-(3-chlorophenyl)-6-isopropyl-6-methyl-2-neopentyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
19. 4,6-dimethyl-6-ethyl-N-(3-iodophenyl)-2-pentadecyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
20. 2-(2-ethylcyclobutyl)-N-(3-trifluoro-methylphenyl-tetrahydro-2H-1,3-thiazine-3-carbothio-amide,
21. 2-(3-isopropylcyclohexyl)-N-[3-(1,1,2,2-tetrafluoroethoxy(phenyl[tetrahydro-2H-1,3-thiazine-3-carbothioamide,
22. N-(3-bromophenyl)-4-ethyl-2-(3-hexylthiophenyl)-6-methyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
23. 2-[3-(5-ethylcylononyl)propyl]-N-(3-fluorophenyl)-4-methyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
24. 5-ethyl-N-(3-trifluoromethylphenyl)-2-[2,2-dimethyl-3-(3-trifluoromethylphenyl)propyl)-tetrahydro-2H-1,3-thiazine-3-carbothioamide,
25. 4-isopropyl-5-methyl-2-[1-phenyl-1-(3,5-dibromophenyl)ethyl]-N-[3-(1,1,2,2-tetrafluoroethoxy)phenyl]tetrahydro-2H-1,3-thiazine-3-carbo-thioamide,
26. 2-(4-ethyl-2-piperidino)-N-(3-fluorophenyl) tetrahydro-2H-1,3-thiazine-3-carbothioamide,
27. N-(3-chlorophenyl)-5-ethyl-2-[2-(3-isopropoxy-2-pyridyl)propyl]tetrahydro-2H-1,3-thiazine-3-carbothioamide,
28. N-(3-chlorophenyl)-4,5-dimethyl-2-(4-piperidinoundecyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide,
29. N-(3-chlorophenyl)-2-[7-(4-isopropyl-piperidino)nonyl]tetrahydro-2H-2,3-thiazine-3-carbothioamide,
30. N-(3-cyanophenyl)-2-[1-methyl-2-(3-isopropyl-2-pyrazinyl)ethyl]tetrahydro-2H-1,3-thiazine-3-carbothioamide,
31. N-(3-iodophenyl)-5-propyl-2-[13-(2-tetrahydrofuryl) tridecy1] tetrahydro-2H-1,3-thiazine-3-carbothioamide,
32. N-(3-cyanophenyl)-2-(3-methoxyphenyl)-6-methyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
33. N-(3-cyanophenyl)-2-phenethyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
34. N-(3-chlorophenyl)-2-[(2-ethyloctyl)-(2-phenylpentyl)amino] tetrahydro-2H-1,3-thiazine-3-carbothioamide,
35. N-(3-cyanophenyl)-7-methoxy-2-(5-propyl-2,6,9-trimethylundecyl)benzothiazoline-3-carbothioamide,
36. 2-(2-isobutoxy-3-propylphenyl)-N-(3-trifluoromethylphenyl)benzothiazoline-3-carbothioamide,
37. 2-(3-chloro-5-ethylthiophenyl)-N-(3-iodophenyl)-5-trifluoromethylbenzothiazoline-3-carbothioamide,
38. N-(3-chlorophenyl)-2-(5,5-diphenyl-pentyl)benzothiazoline-3-carbothioamide,
39. 2-(4-pyridylmethyl)-N-(3-trifluoromethylphenyl)benzothiazoline-3-carbothioamide,
40. 2-[10-(2-ethyl-3-pyridyl)decyl]-5-iodo-N-(3-trifluoromethylphenyl)benzothiazoline-3-carbothioamide,
41. N-(3-bromophenyl)-2-[2-(2,3-dimethyl piperidino)ethyl]benzothiazoline-3-carbothioamide,
42. N-(3-bromophenyl)-4-fluoro-2-(3-morpholinopropyl)benzothiazoline-3-carbothioamide,
42. N-(3-chlorophenyl-4-methyl-2-[9-(2-pyrazinyl)nonyl]benzothiazoline-3-carbothioamide,
44. 2-dodecyl-5-isopropoxy-N-(3-trifluoromethylphenyl)benzothiazoline-3-carbothioamide,
45. N-(3-chlorophenyl)-2-(2,3-dibromophenyl)-benzothiazoline-3-carbothioamide, and
46. N-(3-chlorophenyl)-2-[2-methyl-3-(4-ethylphenyl)propyl]benzothiazoline-3-carbothioamide.

The compounds of formula I are prepared in accordance with methods well known to those having ordinary skill in the art. In general, the compounds can be prepared by reacting an appropriately-substituted thiazolidine, tetrahydro-2H-1,3-thiazine, or benzothiazoline of the formula



II

with an equivalent amount of a suitably-substituted phenyl isothiocyanate of the formula



III

The reaction typically is carried out at ambient temperature for approximately 14 hours in a suitable solvent. If desired, shorter times will result by heating the reaction mixture at an elevated temperature, up to and including the reflux temperature of the reaction mixture. Furthermore, the reaction can be carried out in the presence of a catalytic amount of a tertiary amine or similar compound, such as triethylamine, triethylenediamine, or imidazole. Suitable solvents include, among others, benzene, toluene, the xylenes, chloroform, ethyl acetate, acetonitrile, and the like. Chloroform is the solvent of choice. The reaction mixture then is worked up in accordance with the usual procedures. Typically, the solvent is removed under reduced pressure and the residue recrystallized from a suitable solvent or solvent combination. The most frequently used recrystallization solvents and solvent combinations are benzene, hexane, benzene/hexane, chloroform/hexane, ethyl acetate/hexane, ethanol, and aqueous ethanol.

The phenyl isothiocyanate of formula III starting materials are readily prepared by known methods from the corresponding amines (anilines). For example, the appropriately-substituted amine is reacted with N,N-dimethylthiocarbamoyl chloride in a suitable solvent, such as benzene, toluene, or a xylene. Typically, the reaction is carried out at reflux temperature for approximately 14 hours. The resulting phenyl isothiocyanate normally is isolated and purified by distillation. Alternatively, the appropriately-substituted aniline can be reacted with thiophosgene in chloroform in the presence of aqueous sodium carbonate at a temperature of 10-15°C.

The thiazolidine, tetrahydro-2H-1,3-thiazine, and benzothiazoline of formula II starting materials also are prepared in accordance with known procedures. In general, the appropriate aldehyde or ketone is condensed with the corresponding mercaptoamine. Thus, the use of a mercaptoethylamine yields a thiazolidine, a mercaptopropylamine yields a tetra-hydro-2H-1,3-thiazine, and a 2-aminothiophenol yields a benzothiazoline. When the mercaptoamine is employed as a salt a small amount of base is added to the reaction mixture and the product is washed with base.

The condensation reaction typically is carried out in either benzene or toluene and in the presence of about one-half equivalent of a base such as triethylamine. The water produced by the condensation reaction is removed by azeotropic condensation and is collected in a Dean-Stark trap. The reaction mixture then is washed with aqueous sodium or potassium hydroxide. The product then is isolated and purified in accordance with usual procedures.

With respect to the required aldehydes, ketones, and mercaptoamines, such compounds are either available commercially or readily prepared by known methods. For an excellent summary of typical preparative methods, see R.B. Wagner and H.D. Zook, "Synthetic Organic Chemistry," John Wiley and Sons, Inc., New York, 1965.

The examples which follow illustrate the preparations of representative compounds of formula I. The first five examples illustrate the preparations of various intermediates. In most cases, the product was identified by elemental microanalysis and nuclear magnetic resonance analysis. Unless otherwise stated, all temperatures are given in degrees Celsius.

Example 1. Preparation of 2-Decylthiazolidine.

A mixture of 34 g. of undecylaldehyde and 22.8 g of 2-aminoethanethiol hydrochloride in about 400 ml. of toluene was heated at reflux overnight. The water of condensation was collected in a Dean-Stark trap. The reaction mixture then was washed with aqueous sodium hydroxide and dried over anhydrous magnesium sulfate. After filtering the reaction mixture, the toluene was distilled under reduced pressure. The residue then was vacuum distilled, b.p. 130-8°/0.1 mm, giving 2-decylthiazolidine. The following elemental microanalysis was obtained:

Calculated for $C_{13}H_{27}NS$: C, 68.06; H, 11.86; N, 6.11.
Found: C, 67.81; H, 11.66; N, 6.14.

Example 2. Preparation of 2-(4-bromophenyl)thiazolidine.

The procedure of Example 1 was repeated, except that the reactants consisted of 18.5 g. of 4-bromobenzaldehyde and 27 g of 2-aminoethanethiol hydrochloride, and the reaction mixture also contained 10 ml. of triethylamine. Since removal of solvent left a solid residue, the material was recrystallized from benzene/hexane to give 2-(4-bromophenyl)thiazolidine, m.p. 105-7°. The following elemental analysis was obtained:

Calculated for $C_9H_{10}BrNS$: C, 44.27; H, 4.13;
N, 5.74.
Found: C, 44.50; H, 4.03;
N, 5.74

Example 3. Preparation of 2-phenyltetrahydro-2H-1,3-thiazoline.

The procedure of Example 1 was repeated, except that the reactants consisted of 12.8 g. of benzaldehyde and 11 g. of 3-amino-1-propanethiol, the toluene was replaced with 200 ml. of benzene, and the reaction time was extended to about 65 hours. After the distillation of solvent, an oil remained to which was added 50 ml. of hexane, giving about 15 g. of white crystals of 2-phenyltetrahydro-2H-1,3-thiazoline, m.p. 64-66° (reported, m.p. 65.6—7°). The product was identified by nuclear magnetic resonance analysis only.

Example 4. Preparation of 2-Ethylbenzothiazoline.

The procedure of Example 1 was repeated, except that the reactants consisted of 37.5 g. of 2-aminothiophenol and 17.5 g of propionaldehyde. The residue which remained after the removal of solvent was distilled *in vacuo*,, chromatographed on a silica gel column with toluene as eluant, and redistilled at 94-104°/0.3 mm. to give 2-ethylbenzothiazoline. The following elemental microanalysis was obtained;
Calculated for $C_9H_{11}NS$: C, 65.41; H, 6.71;
N, 8.48.
Found: C, 65.64; H, 6.66;

Example 5. Preparation of 3-Amino-1-propanethiol.

Hydrogen sulfide was bubbled into a solution, cooled in an ice-bath, of 27 g. of sodium methoxide in 200 ml. of methanol to a phenolpthalein end-point. To the reaction mixture then were added, still with ice-bath cooling, another 27 g. of sodium methoxide and 65 g. of 3-chloropropylamine hydrochloride. The reaction mixture was stirred for one hour at 0° and allowed to warm to ambient temperature. The reaction mixture was filtered to remove solids and the methanol was distilled from the filtrate. The residue then was distilled through a short-path distillation head. The distillate, 11 g., b.p. about 150°, solidified immediately. An additional 9.5 g. of product, 3-amino-1-propanethiol, was obtained by extracting the pot residue with methanol and filtering, followed by distillation of methanol-soluble material.

Example 6. Preparation of N-(3-Chlorophenyl)-2-ethyl--3-thiazolidinecarbothioamide.

A mixture of 1.2 g. of 2-ethylthiazolidine and 1.7 g. of *m*-chlorophenyl isothiocyanate in about 100 ml. of chloroform was stirred at ambient temperature for about 64 hours. Hexane was added to the reaction mixture. The solid which precipitated was isolated by filtration and recrystallized from ethanol, giving 2.5 g. (87% of N-(3-chlorophenyl)-2-ethyl-3-thiazolidinecarbothioamide, m.p. 116-8°. The following elemental microanalysis was obtained:
Calculated for $C_{12}H_{15}ClN_2S_2$: C, 50.26; H, 5.24;
N, 9.77.
Found: C, 50.60; H, 5.14;
N, 9.71.
Each of the following compounds was prepared in accordance with the general procedure of Example 6, using the appropriately-substituted thiazolidine and phenyl isothiocyanate. When available, the approximate reaction time, percent yield, metling point, recrystallization solvent, and elemental microanalysis are given for each compound.

Example 7. N-(3-Bromophenyl)-2-ethyl-3-thiazolidine-carbothioamide, 64 hours, 27%, 124–5°, ethanol
Calculated for $C_{12}H_{15}BrN_2S_2$: C, 43.51; H, 4.56;
N, 8.46.
Found: C, 43.31; H, 4.52;
N, 8.54.

Example 8. N-(3-Cyanophenyl)-2-ethyl-3-thiazolidine-carbothioamide, 64 hours, 139–41°, ethanol.
Calculated for $C_{13}H_{15}N_3S_2$: C, 56.29; H, 5.45;
N, 15.15.
Found: C, 55.97; H, 5.60;
N, 15.08

Example 9. N-(3-Chlorophenyl)-2,2-dipropyl-3-thiazolidinecarbothioamide, 16 hours, 55% 106–8°, aqueous ethanol and then benzene/hexane.
Calculated for $C_{16}H_{23}ClN_2S_2$: C, 56.04; H, 6.76; N, 8.17.
Found: C, 56.25; H, 6.47; N, 8.10

Example 10. N-(3-Chlorophenyl)-2-nonyl-3-thiazolidinecarbothioamide, 16 hours, 78%, 102–4°, ethanol.
Calculated for $C_{19}H_{29}ClN_2S_2$: C, 59.27; H, 7.59; N, 7.28
Found: C, 59.21;H, 7.80; N, 7.23.

Example II. N-(3-Chlorophenyl)-2-decyl-3-thiazolidine-carbothioamide, 64 hours, 78%, 94.–6°, ethanol.
Calculated for $C_{20}H_{31}ClN_2S_2$: C, 60.20; H, 7.83; N, 7.02
Found: C, 60.44; H, 7.68; N, 7.04

Example 12. N-(3-Bromophenyl--2-decyl-3-thiazolidine-carbothioamide, 16 hours, 34%, 94–6°, ethanol. The reaction was carried out in benzene, rather than chloroform.
Calculated for $C_{20}H_{31}BrN_2S_2$: C, 54.16; H, 7.05; N, 6.32.
Found: C, 54.14; H, 7.30; N, 6.33

Examplse 13. 2-Decyl-N-(3-iodophenyl–3-thiazolidine-carbothioamide, 16 hours, 53%, 95—6°, ethanol.
Calculated for $C_{20}H_{31}IN_2S_2$: C, 48.98; H, 6.33; N, 5.71.
Found: C, 47.79; H, 6.30; N, 5.72.
C, 48.91; H, 6.10; N, 5.49.

Example 14. N-(3-Chlorophenyl)-2-phenyl-3-thiazolidine-carbothioamide, 88 hours, 54%, 91-3°, benzene/hexane.
Calculated for $C_{16}H_{15}ClN_2S_2$: C, 57.38; H, 4.51; N, 8.37
Found: C, 59.16; H, 4.50; N, 8.05
Found (w/o drying); C, 60.55; H, 4.64; N, 8.04
Found (block dried at 120); C, 51.80; H, 4.52; N, 8.07.
The sample is apparently undergoing decomposition.

Example 15. N-(3-Fluorophenyl)-2-methyl-2-phenyl-3-thiazolidinecarbothioamide, 88 hours, 144-5°, ethanol.
Calculated for $C_{17}H_{17}FN_2S_2$: C, 61.42; H, 5.15; N, 8.43.
Found: C, 61.30; H, 5.29; N, 8.22

Example 16. N-(3-Chlorophenyl)-2-methyl-2-phenyl-3-thiazolidinecarbothioamide, 64 hours, 32% 128–30°C, ethanol.
Calculated for $C_{17}H_{17}ClN_2S_2$: C, 58.52; H, 4.91; N, 8.03
Found: C, 58.24; H, 5.05; N, 7.87.

Example 17. 2-Methyl-2-phenyl-N-(3-trifluoromethylphenyl)-3-thiazolidinecarbothioamide, 16 hours, 45% 146–8°, ethanol.
Calculated for $C_{18}H_{17}F_3N_2S_2$: C, 56.33; H, 4.48; N, 7.32.
Found: C, 56.79; H, 4.85; N, 7.20

Example 18. N-(3-Chlorophenyl)-2-ethyl-2-phenyl-3-thiazolidinecarbothioamide, 16 hours, 6%, 134–5°, ethanol.
Calculated for $C_{18}H_{19}ClN_2S_2$: C, 59.57; H, 5.28; N, 7.72.
Found: C, 59.32; H, 5.28; N, 7.60

Example 19. N-(3-Chlorophenyl)-2-(0tolyl)-3-thiazolidinecarbothioamide, 16 hours, 160-2°, ethanol.
Calculated for $C_{17}H_{17}ClN_2S_2$: C, 58.52; H, 4.91; N, 8.03.
Found: C, 58.27; H, 4.91; N, 8.00.

Example 20. 2-(4-Bromophenyl)-N-(3-chlorophenyl)-3-thiazolidinecarbothioamide, 16 hours, 70%, 144–5°, ethanol.
Calculated for $C_{16}H_{14}BrClN_2S_2$: C, 46.44; H, 3.41; N, 6.77.
Found: C, 46.17; H, 3.42; N, 6.73

Example 21. N-)3-Chlorophenyl)-2-(2,4-dimethylphenyl)-3-thiazolidinecarbothioamide, 64 hours, 83%, 148-9°, ethanol.
Calculated for $C_{18}H_{19}ClN_2S_2$: C, 59.57; H, 5.28; N, 7.72.
Found: C, 59.57; H, 5.09; N, 7.57.

Example 22. 2-Benzyl-N-)3-chlorophenyl)-3-thiazolidine-carbothioamide, 16 hours, 32% 129-31°, ethanol.
Calculated for $C_{17}H_{17}ClN_2S_2$: C, 58.52; H, 4.91; N, 8.03.
Found: C, 58.78; H, 5.19; N, 7.85.

Example 23. N-(3-Chlorophenyl)-2-(3-pyridyl)-3-thiazolidinecarbothioamide, 16 hours, 100%. 162–5°, precipitated with hexane.
Calculated for $C_{15}H_{14}ClN_3S_2$: C, 53.65; H, 4.17; N, 12.56.
Found: C, 53.47; H, 4.17; N, 12.48.

Example 24. Preparation of N-(3-Chlorophenyl)-2-ethyltetrahydro-2H-1,3-thiazine-3-carbothioamide.

A mixture of 2.6 g. of 2-ethyltetrahydro-2H-1,3-thiazine, 3.4 g. of 3-chlorophenyl isothiocyanate, and 30 ml. of benzene was stirred, after an initial exotherm, at ambient temperature for about 64 hours. To the reaction mixture was added about 10 ml. of hexane, which caused white crystals to form. The mixture was washed with hexane. The solid was recrystallized from about 500 ml. of 10:1 hexane: carbon tetrachloride to give N-(3-chlorophenyl)-2-ethyltetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 69–73°. The following elemental microanalysis was obtained:
Calculated for $C_{13}H_{17}ClN_2S_2$: C, 51.90; H, 5.70; N 9.31.
Found: C, 51.61; H, 5.48; N, 9.19.

Example 25. Preparation of N-(3-Bromophenyl)-2-ethyltetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 24 was repeated, except that the reaction mixture consisted of 1.3 g. of 2-ethyltetrahydro-2H-1,3-thiazine, 2.1 g of 3-bromophenyl isothiocyanate, 15 ml. of benzene, and 15 ml. of hexane. A white precipitate formed within minutes of reaction became exothermic. The solid was recrystallized from carbon tetrachloride which contained a little hexane, giving 1.7 g. (49%) of N-(3-bromophenyl-2-ethyltetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 77–9°. The following elemental microanalysis was obtained;
Calculated for $C_{13}H_{17}BrN_2S_2$: C, 45.22; H, 4.96; N, 8.11; S, 18.57.
Found: C, 43.82; H, 5.23; N, 8.16; S, 19.25.

Example 26. Preparation of N-(3-Chlorophenyl)-2-decyltetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 24 was repeated, except that the reactants consisted of 2.4 g. of 2-decyltetrahydro-2H-1,3-thiazine and 1.7 g. of 3-chlorophenyl isothiocyanate. Solvent was distilled under reduced pressure. The residual oil was crystallized from hexane and recrystallized from ethanol to give 2.2 g (53%) of N-(3-chlorophenyl)-2-decyltetra-hydro-2H-1,3-thiazine-3-carbothioamide, m.p. 63–5°. The following elemental microanalysis was obtained:
Calculated for $C_{21}H_{33}ClN_2S_2$: C, 61.06; H, 8.05; N, 6.78; S, 15.52.
Found: C, 60.83; H, 7.08; S, 15.59.

Example 27. Preparation of N-(3-Bromophenyl)-2-decyltetrahydro-2H-1,3-thiazine-3-carbothioamide.

The prcedure of Example 25 was repeated, except that the reactants consisted of 0.9 g of 2-decyltetrahydro-2H-1,3-thiazine and 0.7 g. of 3-bromophenyl isothiocyanate. The product was recrystalized from ethanol to give N-(3-bromophenyl)-2-decyltetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 73-4°. The following elemental microanalysis was obtained:
Calculated for $C_{21}H_{33}BrN_2S_2$; C, 55.13; H, 7.27; N, 6.12; S, 14.02.
Found: C, 55.18; H, 7.03; N, 6.03; S, 13.83.

Example 28. Preparation of N-(3-Chlorophenyl–2-phenyltetrahydro-2H-1, 3-thiazine-3-carbothioamide.

The reactions of 3.6 g. of 2-phenyltetrahydro-2H-1,3-thiazine and 3.4 g. of 3-chlorophenyl isothiocyanate was carried out as described in Example 24, except that the volume of benzene was increased to 40 ml.

and the reaction time was reduced to about 16 hour. A first crop of product was obtained by filtering the reaction mixture and washing the isolated solid with benzene. A second crop was obtained by adding hexane to the filtrate from the first crop isolation. Both crops were recrystallized from ethaol, m.p. 132–5° and 137–8°, respectively, giving a total of 4.6 gm. (66% of N-(3-chlorophenyl-2-phenyltetrahydro-2H-1,3-thiazine-3-carbothioamide. The following elemental microanalysis was obtained:

Calculated for $C_{17}H_{17}ClN_2S_2$; C, 58.52; H, 4.91; N, 8.03; S, 18.38.
Found: C, 58.66; H, 5.17; N, 8.19; S, 18.08.

Example 29. Preparation of N-(3-Bromophenyl)-2-phenyl-tetrahydro-2H-1,3-thiazine-3-carbothioamide.

The reaction of 2.4 g. of 2-phenyltetra-hydro-2H-1,3-thiazine with 2.9 g. of 3-bromophenyl isothiocyanate was carried out as described in Example 24, except that the reaction time was about 16 hours. The reaction mixture was worked up as described in Example 27, giving 4.3 g. (82%) of N-[3-bromophenyl)-2-phenyltetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 135–7°. The following elemental microanalysis was obtained:

Calculated for $C_{17}H_{17}BrN_2S_2$: C, 51.91; H, 4.36; N, 7.12; S, 16.30.
Found: C, 51.87; H, 4.52; N, 6.96; S, 16.39.

Example 30. Preparation of N-(3-Chlorophenyl)-2-(o-tolyl)tetrahydro-2H-2,3-thiazine-3-carbothioamide.

The procedure of Example 24 was repeated, except that the reactants consisted of 1.9 g. of 2-(*o*-tolyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide and 1.7 g. of 3-chlorophenyl isothiocyanate. The product was recrystallized from ethanol to give 3.1 g. (86%) of N-(3-chlorophenyl)-2-(*o*-tolyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 134-6°. The following elemental microanalysis was obtained:

Calculated for $C_{18}H_{19}ClN_2S_2$: C, 59.57; H, 5.28; N, 7.72; S, 17.67.
Found: C, 59.79; H, 5.57; N, 7.59; S, 17.49.

Example 31. Preparation of N,2-Bis(3-chlorophenyl)-tetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 29 was repeated, except that the reactants consisted of 2.1 g of 2-(3-chlorophenyl)tetrahydro-2H-1,3-thiazine and 1.7 g. of 3-chlorophenyl isothiocyanate, giving 3.3 g (86%) of N,2-bis (3-chlorophenyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 151–3°. The following elemental microanalysis was obtained:

Calculated for $C_{17}H_{16}C1_2N_2S_2$: C, 53.26; H, 4.21; N, 7.31; S, 16.73.
Found: C, 53.10; H, 4.18; N, 7.45; S, 16.71.

Example 32. Preparation of 2-(3-Chlorophenyl)-N-(3-trifluoromethylphenyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 29 was repeated, except that the reactants consisted of 1.9 g. of 2-(3-chlorophenyl)tetrahydro-2H-1,3-thiazine and 1.8 g. of 3-trifluoromethylphenyl isothiocyanate, to give 2.7 g. (73%) of 2-(3-chlorophenyl)-N-(3-trifluoromethylphenyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 143-5°. The following elemental microanalysis was obtained:

Calculated for $C_{18}H_{16}ClF_3N_2S_2$: C, 51.86; H, 3.87; N, 6.72; S, 15.38.
Found: C, 51.74; H, 4.01; N, 6.98; S, 15.22.

Example 33. Preparation of 2-(4-Bromophenyl)-N-(3-chlorophenyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 29 was repeated, except that the reactants consisted of 2.6 g. of 2-(4-bromophenyl)tetrahydro-2H-1,3-thiazine and 1.7g. of 3-chlorophenyl isothiocyanate. The product was isolated by filtration, washed with benzene, and recrystallized from chloroform /benzene, giving 3.7 g. (86%) of 2-(4-bromophenyl)-N-(3-chlorophenyl-tetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 144–6°. The following elemental microanalysis was obtained:

Calculated for $C_{17}H_{16}BrClN_2S_2$: C, 47.73; H, 3.77; N, 6.55; S, 14.99.
Found: C, 47.96; H, 3.93; N, 6.50; S, 14.64.

Example 34. Preparation of N-(3-Chlorophenyl)-2-methylbenzothiazoline-3-carbothioamide.

A mixture of 1.5 g. of 2-methylbenzothiazoline, 1.7 g. of 3-chlorophenyl isothiocryanate, about 100 ml. of chloroform, and a catalytic amount of imidazole was heated at reflux for several hours. Since thin layer chromatographic analysis showed that reaction was not complete and that some 3-chlorophenyl isothiocyanate had been lost, an additional 1.3 g. of the isothiocyanate was added to the reaction mixture which then was heated at reflux for about 16 hours. The solvent was distilled under reduced pressure and the residue was recrystallized from ethanol to give N-(3-chlorophenyl)-2-methylbenzothiazoline-3-car-

bothioamide,m.p 120-2°. The following elemental microanalysis was obtained:
Calculated for $C_{15}H_{13}ClN_2S_2$: C, 56.15; H, 4.08; N, 8.73.
Found: C, 55.91; H, 4.09; N, 8.44

Each of the following compounds was prepared in accordance with the general procedure of Example 34, except that a second addition of isothiocyanate was not required. The approximate reaction time and catalyst, if present, are given for each compound. When available, the percent yield, melting point, recrystallization solvent, and elemental microanalysis also are given for each compound.

Example 35. N-(3-Chlorophenyl)-2-ethylbenzothiazoline-3-carbothioamide, 16 hours, 54%, 92–5°, ethanol.
Calculated for $C_{16}H_{15}ClN_2S_2$: C, 57.40; H, 4.48; N, 8.37.
Found: C, 57.80; H, 4.72; N, 8.50

Example 36. N-(3-Bromophenyl)-2-ethylbenzothiazoline-3-carbothioamide, 16 hours, imidazole, 55%, 101–3°, ethanol.
Calculated for $C_{16}H_{15}BrN_2S_2$: C, 50.66; H, 3.99; N, 7.38.
Found: C, 50.55; H, 4.08; N, 7.28.

Example 37. N-(3-Chlorophenyl)-2-isopropylbenzothiazoline-3-carbothioamide, 64 hours, triethylenediamine, 69%, 117–20°, ethanol.
Calculated for $C_{17}H_{17}ClN_2S_2$: C, 58.52; H, 4.91; N, 8.03.
Found: C, 58.82; H, 4.84; N, 7.85.

*Example 38. N-(3-Chlorophenyl)-2-undecylbenzothiazoline-3-carbothioamide,*16 hours, 33% the product was chromatographed on silica gel with toluene as eluant.
Calculated for $C_{25}H_{33}ClN_2S_2$: C, 65.12; H, 7.21; N, 6.08.
Found: C, 65.35; H, 7.17; N, 5.83.

Example 39. N-(3-Chlorophenyl)-2-cyclohexylbenzothiazoline-3-carbothioamide, 64 hours, imidazole, 134–8°, ethanol.
Calculated for $C_{20}H_{21}ClN_2S_2$: C, 61.76; H, 5.44; N, 7.20.
Found: C, 61.70; H, 5.48; N, 7.11.

Example 40. 2-Benzyl-N-(3-chlorophenyl)benzothiazoline-3-carbothioamide, 16 hours, imidazole, 48%, 144–6°, aqueous ethanol.
Calculated for $C_{21}H_{17}ClN_2S_2$: C, 63.54; H, 4.32; N, 7.06.
Found: C, 63.35; H, 4.49; N, 6.97.

Example 41. Preparation of N-(3-Chlorophenyl)-2-methyltetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 24 was repeated, except that the reaction mixture consisted of 0.9 g. of 2-methyltetrahydro-2H-1,3-thiazine, 1.3 g. of 3-chlorophenyl isothiocyanate, 15 ml. of cyclohexane, and 15 ml. of hexane. A white percipitate formed within minutes as the reaction became exothermic. The mixture was stirred at room temperature for 12 hours. The solid was recrystallized from benzene/cyclohexane, giving 1.7 g. of N-(3-chlorophenyl)-2-methyltetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 116–117°C. The following elemental microanalysis was obtained:
Calculated for $C_{12}H_{15}ClN_2S_2$: C, 50.25; H, 5.27; N, 9.77.
Found: C, 50.56; H, 5.54; N, 9.75.

Example 42. Preparation of N-(3-Chlorophenyl)-2-n-propyltetrahydro-2H-1,3-thiazine-3-carbothioamide.

The procedure of Example 41 was repeated, except that the reaction mixture consisted of 1.0 g. of 2-n-propyltetrahydro-2H-1,3-thiazine, 1.2 g. of 3-chlorophenyl isothiocyanate, 15 ml. of cyclohexane, and 15 ml. of hexane. After the recrystallization there was formed 1.9 g. of N-(3-chlorophenyl)-2-n-propyltetrahydro-2H-1,3-thiazine-3-carbothioamide, m.p. 104–106°C. The following elemental microanalysis was obtained:
Calculated for $C_{14}H_{19}ClN_2S_2$: C, 53.40: H, 6.08; N, 8.90
Found: C, 53.39; H, 6.24; N, 8.66.

The compounds of formula I are useful for the control of insect pests. For example, the compounds are active against such insects as Mexican bean beetle, boll weevil, corn rootworm, cereal leaf beetle, borers, Colorado potato beetle, grain beetles, alfalfa weevil, carpet beetle, confused flour beetle, powder post beetle, wireworms, rice weevil, rose beetle, plum curculio, white grubs, melon aphid, rose aphid, white fly, grain aphid, corn leaf aphid, pea aphid mealy-bugs, scales, leafhopper, citrus aphid, spotted alfalfa aphid, green peach aphid, bean aphid, milkweed bug, tarnished plant bug, box elder bug, bed bug,

squash bug, chinch bug, housefly, yellow-fever mosquito, stable fly, horn fly, cabbage maggot, carrot rust fly, codling moth, cutworm, clothes moth, Indian meal moth, leafrollers, corn earworm, European corn borer, cabbage looper, cotton bollworm, bagworm, sod webworm, fall armyworm, German cockroach, and American cockroach.

Because the compounds of formula I appear to function most effectively when ingested by the target insect, such compounds are particularly useful for the control of insect pests on plants, and especially for the control of Mexican bean beetles. In general, however, the compounds of formula I can be applied to or incorporated into any food or water source for the target insect.

Thus, the present invention provides a method for reducing or eradicating a population of the insect species *Epilachna varivestis* which comprises administering to the insect by ingestion an insecticidally-effective amount of a compound of formula I.

The term "insecticidally-effective amount" refers to an amount which results in the inactivation of the insect. Such inactivation can be lethal, either immediately or with delay, or it can be a sublethal inactivation in which the insect is rendered incapable of carrying out one or more of its normal life processes. Thus, the term "reducing or eradicating" means that the compound of formula I can either kill all of the insect species to which the compound is administered, or that the administration of the compound reduces the population of such insect species. As is well known in the art, many known insecticides render the insect incapable of carrying out one or more of its normal life processes. Most often, the nervous system typically is seriously disturbed. However, the precise mechanism by which the compounds of formula I operate is not yet known, and the insecticidal methods of the present invention are not limited by any mode of operation.

The utilization of an inactivating amount of one of the compounds of formula I is critical to the present insecticidal method. The inactivating amount can sometimes be administered by employing the compound in unmodified form. However, for best results, it generally is necessary that the compound or compounds be employed in modified form; that is, as one component of a composition formulated to implement the insecticidal effects. Thus, for example, the active ingredient can be mixed with water or other liquid or liquids, preferably aided by the usage of a surface-active agent. The compounds also can be incorporated on finely-divided solid, which can be a substance having surface-active adsorption properties, to yield a wettable powder which subsequently can be dispersed in water or other liquid, or incorporated as part of a dust which can be applied directly. Other methods of formulation are known in the art and can be employed in implementing the present invention.

The exact concentration of one or more of the compounds of formula I in a composition thereof with one or a plurality of adjuvants can vary; it is necessary only that one or more of the products be present in such amount as to make possible the application of an inactivating dosage to an insect. In many situations, a composition comprising about 0.001 percent by weight of the present active agent of formula I is effective for the administration of an inactivating amount thereof to insect pests. Compositions having a higher concentration of active agent of formula I, such as a concentration of from about 0.001 to about 0.5 percent can, of course, be employed. In still other operations, compositions containing from about 0.5 to about 98 percent by weight of one or more compounds of formula I are conveniently employed. Such compositions can therefore have a range from 0.001 to 98 percent by weight and are adapted to be employed as treating compositions *per se* or as concentrates for subsequent dilution with additional adjuvant to product ultimate treating compositions.

Liquid compositions containing the desired amount of active agent of formula I are prepared by dissolving the substance in an organic liquid or by dispersing the substance in water with or without the aid of a suitable surface-active dispersing agent such as an ionic or nonionic emulsifing agent. Such compositions also can contain modifying substances which serve to aid spreading and adhesion of the material on plant foliage. Suitable organic liquid carriers include the agricultural spray oils and the petroleum distillates such as diesel fuel, kerosine, fuel oil, naphthas, and Stoddard solvent. Among such liquids the petroleum distillates are generally preferred. The aqueous compositions can contain one or more water-immiscible solvents for the toxicant compound. In such aqueous compositions, the carrier comprises an aqueous emulsion, *e.g.*,, a mixture of water, emulsifying agent, and water-immiscible solvent. The choice of dispersing and emulsifying agent and the amount thereof employed is dictated by the nature of the composition and by the ability of the agent to facilitate the dispersing of the active agent in the carrier to produce the desired composition. Dispersing and emulsifying agents which can be employed in the compositions include the condensation products of alkylene oxides with phensols and organic acids, alkaryl sulfonates, polyoxyalkylene derivates of sorbitan esters, complex ether alcohols, and the like. For a review of known surface-active agents which are suitably employed in implementing the present invention, attention is directed to U.S. Patent No. 3,095,299, second column, lines 25—36, and references cited therein.

In the preparation of dust compositions, the active ingredient of formula I is intimately dispersed in and on a finely-divided solid such as clay, talc, chalk, gypsum, limestone, vermiculite fines, perlite, and the like. In one method of achieving such dispersion, the finely divided carrier is mechanically mixed or ground with the active agent.

Similarly, dust compositions containing the toxicant compounds can be prepared with various of solid carriers such as bentonite, fuller's earth, attapulgite, and other clays having surface-active adsorption properties. Depending upon the proportions of ingredients, these dust compositions can be employed as

concentrates and subsequently diluted with additional adsorptive-type solid carriers or with chalk, talc, or gypsum, or the like to obtain the desired amount of active ingredient in a composition adapted to be employed in accordance with the present invention. Also, such dust compositions can be dispersed in water, with or without the aid of a dispersing agent, to form spray mixtures.

The compositions of the present invention also can be employed in granular formulations. These formulations are prepared in conventional manner, typically by dissolving the compound of formula I in a solvent with or without a surface-active agent and spraying or otherwise distributing the resulting solution onto pre-formed granules. Such granular formulations are capable of providing longer-lasting activity and may be preferred for crops such as corn where repeated application is not practical.

When operating in accordance with the present invention, one or more of the compounds of formula I or a composition containing one or more of the compounds of formula I is applied to a source of food or water for the pest to be controlled in any convenient manner, for example, by means of hand dusters or sprayers or by simple mixing with the food to be ingested by the pest. Application to the foliage of plants is conveniently carried out with power dusters, boom sprayers, and fog sprayers. In such foliar applications, the employed composition should not contain any appreciable amounts of any phytotoxic diluents. In large-scale operations, dust or low volume sprays can be applied from the air. The present invention also comprehends the employment of compositions comprising one or more compounds of formula I, an adjuvant, and one or more other biologically-active materials, such as other insecticides, fungicides, miticides, bacteriocides, nematocides, and the like.

It is usual in describing foliar applications of plant protectants to measure the application rate by the concentration of dispersion in which it is applied. The application rate is measured in this way because it is customary to apply a sufficient amount of the dispersion to cover the foliage with a thin film. The amount of dispersion applied is thus dependent on the foliar area of the plant, and the quantity of plant-protecting compound is dependent upon its concentration in the dispersion.

Thus, in one embodiment, the insecticidal method is carried out by applying the compounds of formula I to the foliage of plants or other source of food for the insect, and applications are made in the same manner as already described. The insecticidal appplication rates are from about 100 ppm to about 2000 ppm. It is, of course, apparent that higher or lower concentrations can be employed, depending upon the insect species to be controlled, the plant or other food source to which application is to be made, and the potency or toxicity of the particular compound in the composition.

The activity of representative compounds of formula I against Mexican bean beetle is illustrated by the following example.

Example 41

The compounds to be tested were dissolved or suspended in 50:50 acetone: ethanol, and a blend of anionic and nonionic surfactants was added. The solution then was dispersed in water, so that the final dispersion contained about 20 percent of solvent and the concentration of test compound shown in the table below.

The test compound dispersions were sprayed on the foliage of young bean plants in an amount sufficient to wet the foliage completely. The dispersions then were allowed to dry, and individual leaves were removed from the plants. The petiole of each leaf was wrapped in water-soaked cotton and the leaf then was infested with second instar larvae of Mexican bean beetle. Five larvae were applied to each leaf, and two replicates were used for each compound concentration. Mortality was observed on the fourth and seventh days after treatment.

Untreated control insects were included with every group of test insects.

Insect mortality produced by the compound was rated on a scale where 0 represented no mortality, 1 represented less than 50 percent mortality, 2 represented 51-99 percent mortality, and 3 represented 100 percent mortality of insects. Results were averaged where a compound was tested repeatedly against the insect. Empty spaces in the table indicate that the compound was not tested at the indicated rate. The results produced by typical compounds of formula I are summarized in table 1 which follows.

TABLE 1

ACTIVITY OF REPRSENTATIVE COMPOUNDS AGAINST MEXICAN BEAN BEETLE

	ORIGINAL TEST							RETEST	
Compound of Example	1000 ppm. 4 days	1000 ppm. 7 days	100 ppm. 4 days	100 ppm. 7 days	100 ppm. 7 days	50 ppm. 7 days	25 ppm. 7 days	10 ppm. 7 days	5 ppm. 7 days
6	3	3	3	3	3	3	3	0	
7	3	3	3	3	3	3	3	1	
8	3	3	0	1	3	3	2	1	
9			3	3	3	3	3	1	
10	3	3	0	0					
11	3	3	0	0					
12			2	3	3	2	1	1	
13			1	3	2			1	
14	3	3	1	2					
15	0	0	1	1					
16	3	3	1	2					

TABLE 1 (Continued)

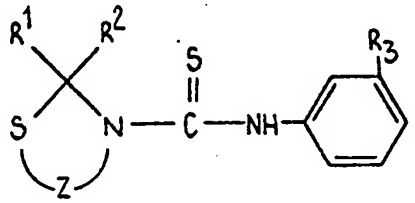
Compound of Example	ORIGINAL TEST				RETEST				
	1000 ppm.		100 ppm.		100 ppm.	50 ppm.	25 ppm.	10 ppm.	5 ppm.
	4 days	7 days	4 days	7 days	7 days	7 days	7 days	7 days	7 days
17	0	3	0	1					
18	1	3	0	0					
19	2	3	0	0					
20	0	0	0	0					
21	2	3	0	1					
22			2	3	3	3	3		
23	0	0	0	0					
24	3	3	3	3	3	2	2		
25	3	3	3	3					
26	3	3	3	3	3			1	
27	3	3	3	3					
28	3	3	3	3	3	3	1		

TABLE 1 (Continued)

Compound of Example	ORIGINAL TEST 1000 ppm. 4 days	1000 ppm. 7 days	100 ppm. 4 days	100 ppm. 7 days	100 ppm. 7 days	50 ppm. 7 days	25 ppm. 7 days	RETEST 10 ppm. 7 days	5 ppm. 7 days
29	3	3	3	3	3	3	3	2	
30	3	3	3	3	3	3	3	1	
31	3	3	3	3	3			0	
32	3	3	3	3	3			1	
33	2	3	3	3	3			1	
34	3	3	1	3	3	3	1		
35	3	3	3	3	3	3	3	1	
36	3	3	2	3	3	3	3	2	0
37	3	3	3	3	3	3	3	0	
38	0	3	0	1	3	3	2	1	
39	3	3	1	2					
40	3	3	1	1					

CLAIMS

1. A compound of the general formula,



wherein

R^1 is

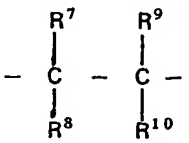
(A) C_1–C_{18} alkyl;
(B) C_2–C_{18} alkenyl;
(C) C_4–C_{18} alkadienyl;
(D) C_3-C_{12} cycloalkyl, optionally substituted with either one or two C_1–C_3 alkyl groups;
(E) C_5–C_{12} cycloalkenyl, optionally substituted with either one or two C_1–C_3 alkyl groups;
(F) C_6-C_{12} cycloalkadienyl, optionally substituted with either one or two C_1-C_3 alkyl groups;
(G) phenyl, optionally substituted with from one to three groups selected from the group consisting of
(1) C_1–C_6 alkyl,
(2) C_1–C_6 alkoxy,
(3) C_1–C_6 alkylthio,
(4) trifluoromethyl,
(5) halo, and
(6) cyano
(H) (cycloalkyl)alkyl, containing no more than about 18 carbon atoms, in which the cycloalkyl moiety is as defined hereinabove;
(I) phenylalkyl, containing no more than about 18 carbon atoms, in which the phhenyl moiety is as defined hereinabove;
(J) diphenlalkyl, containing no more than about 18 carbon atoms, in which each phenyl moiety is as defined hereinabove;
(K) pyridyl, optionally substituted with either one or two groups selected from the group consisting of
(1) C_1–C_3 alkyl,
(2) C_1–C_3 alkoxy, or
(3) halo;
(L) piperidino attached at a position other than the nitrogen atom, optionally substituted with either one or two C_1–C_3 alkyl groups;
(M) morpholino attached at a position other than the nitrogen atom;
(N) pyrazinyl, optionally substituted with either one or two C_1–C_3 alkyl groups;
(O) pyridyalkyl, contaning no more than about 18 carbon atoms, in which the pyridyl moiety is as defined hereinabove;
(P) piperidinoalkyl, containing no more than about 17 carbon atoms, in which the piperidino moiety is as defined hereinabove.
(Q) morpholinalkyl, containing no more than about 16 carbon atoms;
(R) pyrazinylalkyl, containing no more than about 16 carbon atoms, in which the pyrazinyl moiety is as defined hereinabove; or
(S) tetrahydrofurylalkyl, containing no more than about 17 carbon atoms;

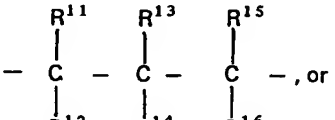
R^2 is hydrogen or C_1—C_3 alkyl;

R^3 is

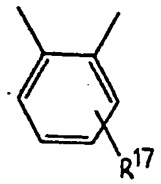
(A) halo,
(B) trifluoromethyl,
(C) cyano, or
(D) 1,1,2,2-tetrafluoroethoxy;

Z is

(A) 

(B) 

(C)

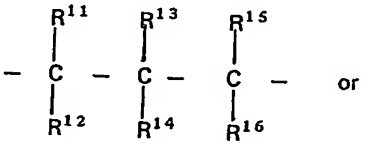


in which each of R^7-R^{16}, inclusive, independently is hyrogen or C_1-C_3 alkyl, with the proviso that the two groups attached to any given carbon atom in (A(or (B) together can not contain more than four carbon atoms; and

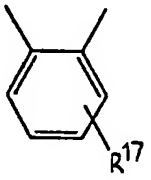
R^{17} is

(1) C_1–C_3 alkyl,
(2) C_1–C_3 alkoxy,
(3) C_1–C_3 alkylthio,
(4) trifluoromethyl,
(5) halo,
(6) cyano, or
(7) hydrogen;

with the proviso that when Z is

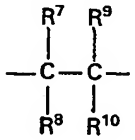


or



R^2 is hydrogen.

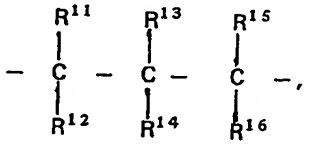
2. a Compound of Claim 1, wherein R^1 is alkyl, phenyl, optionally monosubstituted with halo or C_1–C_3 alkyl,; or phenylalkyl in which the phenyl moeity is unsubstituted.
3. A compound of Claim 1, wherein R^3 is halo or trifluoromethyl.
4. A compound of Claim 1, wherein each of R^7-R^{17}, inclusive, is hydrogen.
5. A compound of Claim 4, wherein Z is



;

R^1 is alkyl; benzyl; or phenyl, optionally monosubstituted with bromo; and R^3 is chloro or bromo.

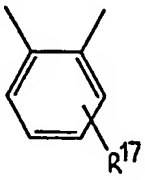
6. A compound of Claim 4, wherein Z is



,

R^1 is alkyl, or phenyl, optionally monosubstituted with methyl, bromo, or chloro; R^2 is hydrogen; and R^3 is bromo, chloro, or trifluoromethyl.

7. A compound of Claim 4, wherein Z is

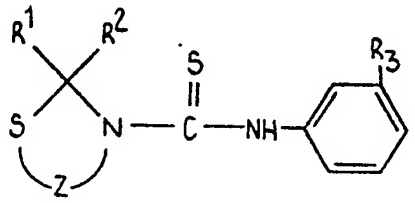


R^1 is C_1–C_3 alkyl; R^2 is hydrogen; and R^2 is bromo or chloro.

8. Any one of the following compounds of Claim 1:

N-(3-bromophenyl)-2-ethyl-3-thiazolidine-carbothioamide,
N-(3-chlorophenyl)-2-ethyl-3-thiazolidine-carbothioamide,
M-(3-chlorophenyl)-2,2-dipropyl-3-thiazolidinecarbothioamide,
2-benzyl-N-(3-chlorophenyl)-3-thiazolidine-carbothioamide,
N-(3-bromophenyl)-2-ethyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
N-(3-bromophenyl)-2-decyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
N-(3-bromophenyl)-2-phenyltetrahydro-2H-1,3-thiazine-3-carbothioamide,
N-(3-chlorophenyl)-2-(2-methylphenyl-tetrahydro-2H-1,3-thiazine-3-carbothioamide,
2,N-bis(3-chlorophenyl)tetrahydro-2H- 1,3-thiazine-3-carbothioamide,
2-(3-chlorophenyl)-N-(3-trifluoromethyl-phenyl)tetrahydro-2H-1,3-thiazine-3-carbothioamide,
N-(3-chlorophenyl)-2-methylbenzothiazoline-3-carbothioamide,
N-(3-bromophenyl)-2-ethylbenzothiazoline-3-carbothioamide,
N-(3-chlorophenyl)-2-ethylbenzothiazoline-3-carbothioamide,

9. A process for prearing a compound of the general formula,



wherein

R^1 is

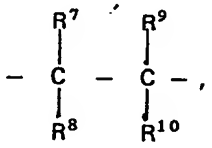
(A) C_1–C_{18} alkyl;
(B) C_2–C_{18} alkenyl;
(C) C_4–C_{18} alkadienyl;
(D) C_3–C_{12} cycloalkyl, optionally substituted with either one or two C_1–C_3 alkyl groups;
(E) C_5–C_{12} cycloalkenyl, otpionally substituted with either one or two C_1–C_3 alkyl groups;
(F) C_6–C_{12} cycloalkadienyl, optionally substituted with either one or two C_1–C_3 alkyl groups;
(G) phenyl, optionally substituted with from one to three groups selected from the group consisting of
(1) C_1–C_6 alkyl,
(2) C_1–C_6 alkoxy,
(3) C_1–C_6 alkylthio,
(4) trifluoromethyl,
(5) halo, and
(6) cyano;
(H) (cycloalkyl)alkyl, containing no more than about 18 carbon atoms, in which the cycloalkyl moiety is as defined hereinabove;
(I) phenylalkyl, containing no more than about 18 carbon atoms, in which the phenyl moiety is as defined hereinabove;
(J) diphenylalkyl, containing no more than about 18 carbon atoms, in which each phenyl moiety is as defined hereinabove;
(K) pyridyl, optionally substituted with either one or two groups selected from the group consisting of
(1) C_1–C_3 alkyl,
(3) C_1–C_3 alkoxy, or
(3) halo;
(L) piperidino attached at a position other than the nitrogen atom, optionally substituted with either one or two C_1–C_3 alkyl groups;
(M) morpholino attached at a position other than the nitrogen atom;
(N) pyrazinyl, otpionally substituted with either one or two C_1–C_3 alkyl groups;
(O) pyridylalkyl, containing no more than about 17 carbon atoms, in which the pyridyl moiety is as defined hereinabove;
(P) piperidinoalkyl, containing no more than about 18 carbon atoms, in which the piperidino moiety is as defined hereinabove;
(Q) morpholinalkyl, containing no more than about 16 carbon atoms;
(R) pyrazinlalkyl, containing no more than about 16 carbon atoms, in which the pyrazinyl moiety is as defined hereinabove; or
(S) tetrahydrofurylalkyl, containing no more than about 17 carbon atoms;

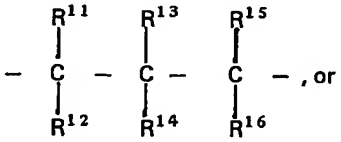
R^2 is hydrogen or C_1–C_3 alkyl;

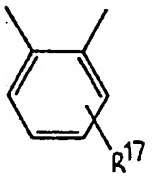
R^3 is

(A) halo,
(B) trifluoromethyl
(C) cyano, or
(D) 1,1,2,2-tetrafluoroethoxy;

Z is

(A) 

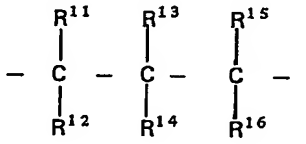
(B) 

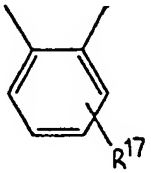
(C) 

in which each of R^7-R^{16}, inclusive, independently is hydrogen or C_1–C_3 alkyl, with the proviso that the two groups attached to any given carbon atom in (A(or (B) together can not contain more than four carbon atoms; and

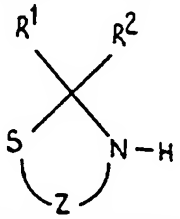
R^{17} is

(1) C_1–C_3 alkyl,
(2) C_1–C_3 alkoxy,
(3) C_1–C_3 alkylthio,
(4) trifluoromethyl,
(5) halo,
(6) cyano, or
(7) hydrogen; with the proviso that when Z is

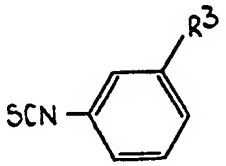
 or



R^2 is hydrogen; which comprises reacting a compound of the formula



wherein R^1, R^2, and Z are defined as before, with a phenyl isothiocyanate of the formula



wherein R^3 is defined as before.

10. An insecticidal composition which comprises an insecticidally-effective amount of a compound of Claims 1–8 and an agriculturally-acceptable carrier.

11. A composition of claim 10 wherein the insecticidaly-effective amount of active ingredient is from about 0.001 to 98 percent by weight.

12. A method for reducing or eradicating a population of an insect species which comprises applying to the insect or its habitat a compound as defined in any of claims 1 to 8.

13. A compound as claimed in Claim 1 substantially as hereinbefore described with particular reference to any one of the Examples.

14. A process as claimed in Claim 9 substantially as hereinbefore described with particular reference to any one of the Examples.

15. An insecticidal composition as claimed in Claim 10 substantially as hereinbefore described.

16. A method as claimed in claim 12 substantially as hereinbefore described.

17. A compound as claimed in any of claims 1 to 8, for use as an insecticide.

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